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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
|-----------------|-------------|----------------------|---------------------|------------------|

10/803,195

03/18/2004

Richard J. Feldmann

3399-Z

6156

7590

02/28/2007

Law Office of Jim Zegeer
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Alexandria, VA 22314

EXAMINER

BRUSCA, JOHN S

ART UNIT

PAPER NUMBER

1631

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
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3 MONTHS

02/28/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/803,195

Applicant(s)

FELDMANN, RICHARD J.

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Priority

1. The objection to the priority claim in the Office action mailed 14 June 2006 is withdrawn in view of the amendment to the specification filed 14 December 2006.
2. The attempt to claim priority under 35 U.S.C. 120 to International application No. PCT/US01/16471 and Application Nos. 10/339,666, 10/364,516, and 10/364,412 is improper because the relationships between the claimed applications and the instant application are not stated and the claim for priority was not timely.

A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR

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1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

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3. Acknowledgment is made of applicant's claim for foreign priority based on International application No. PCT/US01/16471 filed on 31 May 2001. It is noted, however, that applicant has not filed a certified copy of the International application as required by 35 U.S.C. 119(b).

Specification

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR §§ 1.821(a)(1) and (a)(2).

However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the following reasons:

Several nucleotide sequences appear in the specification on pages 3, 22-42, 44, 45, and figures 5 and 6 that are not properly identified. Nucleotide sequences must be identified by sequence identification number. Furthermore, if said sequences do not appear in the sequence listing, a new listing including said sequences must be supplied. It is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP 2422.02). If said sequences consist of a portion of sequences already of record in the sequence listing, they may be identified in the specification using the existing SEQ ID No. accompanied by the position of the sequence on the already listed sequence.

Applicants are required to comply with all the requirements of 37 CFR §§ 1.821-1.825. Any response to this Office Action which fails to meet all of these requirements will be considered non-responsive. The nature of the sequences disclosed in the instant application has allowed an examination on the merits, the results of which are communicated below.

5. It is noted that the statement "included by reference" on pages 4 and 8 are not sufficient to incorporate by reference a prior art reference (see MPEP 608.01(p)).

Claim Rejections - 35 USC § 101

6. The rejection of claims 1-16 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter in the Office action mailed 14 June 2006 is withdrawn in view of the amendment to the claims filed 14 December 2006.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) Quantity of experimentation: The only utility asserted by the specification is to use connectron symmetries to predict control of gene expression (see for example page 8 of the

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specification and the preamble of claims 1-8). In order to practice the claimed invention one of skill in the art must identify and use a connectron to predict regulation of gene expression. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The amount of direction or guidance presented: The claimed invention is a method of identification of sequences that have a connectron relationship and act to modulate gene expression. On pages 9-13 the specification defines connectrons as a tetradic structure between two sequences in an RNA transcript of a genomic sequence and two sequences in double stranded genomic DNA. The specification speculates without evidence that triple-stranded (triplex) structures will form between RNA and double stranded DNA in chromatin where connectron symmetries are identified. The specification does not provide guidance that there are any limitations on formation of triplex structures, and only implies that regions of RNA with identical sequence to one strand of a double stranded DNA sequence will form triplex structures. The specification does not address why all RNA transcripts of genes would not form a continuous triplex structure with the gene from which it is transcribed. The specification provides guidance to identify connectron symmetries in genomic sequences on pages 16-17. The specification does not provide detailed guidance to use identified connectron symmetries because the specification does not show whether or not connectrons form within cells or have an effect on gene expression. The specification does not provide specific guidance for monitoring or effecting changes in connectron behavior that correlate with gene expression.

c) The presence or absence of working examples: The specification provides working examples of identification of connectron symmetries by computer-mediated searching of

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genomic sequences. However, the specification does not provide evidence that connectron symmetries in genomic sequences result in formation of triplex RNA-DNA structures or that if connectron triplex structures do exist that connectrons control gene expression. The specification does not provide working examples of using identified connectron symmetries to predict effects on gene expression. The specification does not provide working examples of monitoring or effecting changes in connectron behavior that correlate with gene expression.

d) The nature of the invention: The nature of the invention, gene expression control, is complex.

e) The state of the prior art: One of skill in the art, after reading the specification, would not know that connectron symmetries identified by computer-mediated searches of genomic sequences would allow for prediction of gene expression of genes that have connectron symmetries. The specification does not provide experimental evidence that connectron symmetries cause modulation of gene expression. Neither the prior art nor post-filing art shows connectrons. Mattick reviews effects of RNA molecules on gene regulation. Mattick does not show connectrons as defined in the instant specification. Chan et al. reviews triplex DNA formation. Chan et al. shows in figures 1A-C that short stretches of oligonucleotides may form parallel or antiparallel triplex structures. Chan et al. shows in figures 1B that parallel triplex forming oligonucleotides form bonds between C and T residues of the oligonucleotide and G and A residues of the double stranded DNA molecule. Figure 1C shows that antiparallel triplex forming oligonucleotides form bonds between A, G, and T residues of the oligonucleotide and A, G, and A residues of the double stranded DNA. Chan et al. characterize the limited range of base pairing possibilities in triplex structures as pyrimidine binding motifs or purine binding motifs.

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Chan et al. describe on pages 268-273 the unpredictability and difficulty of forming desired triplex structures that are limited to the purine motif or the pyrimidine motif. Chan et al. does not show a mechanism that allows for triplex structures to form with any and all regions of identity between an RNA transcript and a region of double stranded DNA that has an identical sequence in one of the two strands of DNA, as required for connectron formation as defined in the instant specification.

f) The relative skill of those in the art: The skill of those in the art of gene expression is high.

g) The predictability of the art: The predictability of the relationship of connectron symmetries and gene expression is unknown in the prior art and is not described in the instant specification.

h) The breadth of the claims: The claims are broad in that they are drawn to identification and design of connectron symmetries whose relationship to gene expression is not established.

The skilled practitioner would first turn to the instant specification for guidance in using the claimed invention. However, the specification lacks any evidence that connectrons form in cells or that connectron symmetries are related to gene expression. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not discuss connectron symmetries. Chan et al. shows that triplex formation occurs only with oligonucleotides with a purine rich or pyrimidine rich motif, rather than with any identical sequence as suggested in the specification. Finally, said practitioner would turn to trial and error experimentation to determine a relationship between connectron symmetries and gene expression. Such amounts to undue experimentation.

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Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on 571 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSB. Brusca 22 February 2007

John S. Brusca
Primary Examiner
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jsb